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Authors Schilter_B Noldner_M Chatterjee_S_S Honegger_P

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Article title	In Vitro Cellular Models for Cardiac Development and Pharmacotoxicology
Article identifier	0887233395100613
Authors	Wobus_A_M Rohwedel_J Maltsev_V Hescheler_J
Journal title	Toxicology in Vitro
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4 ANSWER 3 OF 3 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 2
AN 1999263952 EMBASE
TI Prevalidation of the Embryonic **Stem** Cell Test (EST) - A new in
vitro embryotoxicity test.
AU Scholz G.; Genschow E.; Pohl I.; Bremer S.; Paparella M.; Raabe H.;
Southee J.; Spielmann H.
CS G. Scholz, ZEBET, Federal Institute Health Protection, Consumers and
Veterinary Medicine, Berlin, Germany
SO Toxicology in Vitro, (1999) 13/4-5 (675-681).

Refs: 18
ISSN: 0887-2333 CODEN: TIVIEQ
PUI S 0887-2333(99)00046-6
CY United Kingdom
DT Journal; Conference Article
FS 021 Developmental Biology and Teratology
037 Drug Literature Index
052 Toxicology

LA English

SL English

not here *☆*

AB Pluripotent embryonic **stem** cells (ES cells) of the mouse
(cell-line D3) can be maintained in the undifferentiated state in the
presence of LIF (Leukaemia Inhibitory Factor). Upon withdrawal of LIF,
these cells differentiate into various cell types under appropriate
conditions. This property of ES cells allowed us to develop an in vitro
embryotoxicity test, the Embryonic **Stem** Cell Test (EST; In Vitro
Toxicology 1997, 10, 119-127), which does not require taking embryonic
cells or tissues from pregnant animals. In the EST, the effect of test
chemicals on three endpoints is assessed: inhibition of the
differentiation of ES cells into contracting myocard, cytotoxicity in ES
cells and cytotoxicity in mouse 3T3 fibroblasts, which are serving as
differentiated cells in the test. The results of a prevalidation study of
the EST are described, which was conducted according to the ECVAM
prevalidation scheme. In the first stage of the study (Phase I), a
standard operating procedure (SOP) was elaborated. In the second phase
(Phase II), the interlaboratory transferability of the EST was assessed
using three test chemicals representing three classes of embryotoxicity

(a strong, a weak and a non-embryotoxic chemical) in two European
laboratories (**ZEBET** at the BgVV in Berlin, Germany; ECVAM at the
JRC in Ispra, Italy) and one US laboratory (Institute for In Vitro
Sciences (IIVS) in Gaithersburgh, MA, USA). In the final stage of
prevalidation (Phase III), nine test chemicals and a positive control

were tested under blind conditions at **ZEBET** and ECVAM. The
statistical evaluation of the results led to the development of an
improved prediction model for the EST. Copyright (C) 1999 Elsevier
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L16 ANSWER 3 OF 8 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 2
AN 95259045 EMBASE
DN 1995259045
TI In vitro cellular models for cardiac development and pharmacotoxicology.
AU Wobus A.M.; Rohwedel J.; Maltsev V.; Hescheler J.
CS Inst. Pflanzengen./Kulturpflanzenf., Corrensstr. 3,D-06466 Gatersleben,
Germany
SO Toxicology in Vitro, (1995) 9/4 (477-488).
ISSN: 0887-2333 CODEN: TIVIEQ
CY United Kingdom
DT Journal; Conference Article
FS 018 Cardiovascular Diseases and Cardiovascular Surgery
021 Developmental Biology and Teratology
030 Pharmacology
037 Drug Literature Index
052 Toxicology
LA English
SL English
AB Permanent cultures of cardiac cells described so far have limited value
for studying cell biology and pharmacology of the developing heart
because
of the loss of proliferative capacity and cardiac-specific properties of
cardiomyocytes during long-term cultivation. Pluripotent embryonic
carcinoma (EC) and embryonic stem (ES) cells cultivated as permanent
lines
offer a new approach for studying cardiogenic differentiation in vitro.
We
describe cardiogenesis in vitro by differentiating EC and ES cells by way
of embryo-like aggregates (embryoid bodies) into spontaneously beating
cardiomyocytes. During cardiomyocyte differentiation three distinct
developmental stages were defined by expression of specific action
potentials and ionic currents measured by the whole-cell patch-clamp
technique. Whereas early differentiated cardiomyocytes are characterized
by action potentials and ionic currents typical for early pacemaker
cells,
terminally differentiated cardiomyocytes show action potentials and ionic
currents inherent to ventricular-, atrial- or sinus nodal-like cells.
These functional characteristics are in accordance with the expression of
.alpha.- and .beta.-cardiac myosin heavy chain at early differentiation
stages and the additional expression of ventricular-specific MLC-2V and
atrial-specific ANF genes at terminal stages demonstrated by reverse
transcription polymerase chain reaction (RT-PCR) analysis.
Pharmacological
studies performed by measuring chronotropic responses and by analysing
the
Ca²⁺ channel activity correspond to data obtained with cardiac cells from
living organisms. For testing the influence of exogenous compounds on
cardiac differentiation the **teratogenic** compound retinoic acid
(RA) was applied during distinct stages of **embryoid body**
development. A temporally controlled influence of RA on cardiac
differentiation and expression of cardiac-specific genes was found. We
conclude that ES cell-derived cardiomyocytes provide an excellent
cellular
model to study early cardiac development and to perform pharmacological
and embryotoxicological investigations.

=> d his

(FILE 'HOME' ENTERED AT 08:59:18 ON 12 JUL 2001)

FILE 'MEDLINE' ENTERED AT 08:59:28 ON 12 JUL 2001

L1 74 S EMBRYOID BODY/AB,BI
L2 3 S L1 AND (TOXIC? OR TERATOGEN?)/AB,BI
L3 80 S (EMBRYONIC STEM OR PRIMORDIAL GERM) AND (TERATOGEN? OR
TOXIC?
L4 25 S L3 AND EXPRESSION/AB,BI

FILE 'STNGUIDE' ENTERED AT 09:02:30 ON 12 JUL 2001

FILE 'MEDLINE' ENTERED AT 09:10:09 ON 12 JUL 2001

L5 19 S L1 AND (TEST? OR ASSAY?)/AB,BI

FILE 'STNGUIDE' ENTERED AT 09:11:14 ON 12 JUL 2001

FILE 'MEDLINE' ENTERED AT 09:17:28 ON 12 JUL 2001

L6 3049 S L1 OR EMBRYONIC STEM OR PRIMORDIAL GERM/AB,BI
L7 131 S L6 AND DRUG# AND (ASSAY? OR PROFILE# OR TEST?)/AB,BI
L8 53 S L7 AND EXPRESSION/AB,BI
L9 49 S L8 AND (PROTEIN# OR GENE#)/AB,BI

FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS' ENTERED AT 09:28:40 ON

12

JUL 2001

E SNODGRASS H/AU
L10 149 S E3 OR E10 OR E11
L11 3 S L10 AND EMBRYOID BOD?/AB,BI
L12 2 DUP REM L11 (1 DUPLICATE REMOVED)
L13 17 S L10 AND (EMBRYONIC STEM OR PRIMORDIAL GERM)/AB,BI
L14 8 DUP REM L13 (9 DUPLICATES REMOVED)
L15 19 S L2
L16 8 DUP REM L15 (11 DUPLICATES REMOVED)
L17 248091 S EMBRYOID OR EMBRYONIC OR PRIMORDIAL/AB,BI
L18 4528 S L17 AND PROFIL?/AB,BI
L19 646 S L18 AND (DRUG# OR TOXI? OR TERATOGEN?)/AB,BI
L20 173 S L19 AND (TEST? OR ASSAY?)/AB,BI
L21 15 S L20 AND SCREEN?/AB,BI
L22 11 DUP REM L21 (4 DUPLICATES REMOVED)
L23 24 S L20 AND (PROTEIN EXPRESSION OR GENE EXPRESSION)/AB,BI
L24 22 DUP REM L23 (2 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 09:43:08 ON 12 JUL 2001

=> d his

(FILE 'HOME' ENTERED AT 11:44:08 ON 12 JUL 2001)

12 FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS' ENTERED AT 11:44:18 ON
JUL 2001

L1 25 S EMBRYONIC STEM CELL TEST/AB, BI
L2 11 DUP REM L1 (14 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 11:45:05 ON 12 JUL 2001